REMARKS

Claims 1, 2, 4, 8 – 11, 13, 14, and 17 - 24 are pending in the application. Claims 1, 8 - 11, 18 and 24 have been amended. Claims 3, 5 – 7, 12, 15, 16 and 23 have been cancelled. No new claims have been added. No new matter has been added by virtue of the amendments and claims, support being found throughout the specification and claims as originally filed. Support for the amendment to claim 1 can be found in the specification, for example at p. 5, lines 8 – 19 or p. 6, lines 8 – 18.

Any cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Claim Objections

Claims 1 and 8 are objected to for minor informalities. (Office Action, p.2). Applicants have amended the claims to correct the minor informalities.

Applicants respectfully request that the objections be withdrawn.

Claim Rejections

35 USC 112, First Paragraph

Claims 1 – 2, 4, 8 – 11, 13 – 14 and 17 - 24 have been rejected under 35 USC 112, first paragraph. The Examiner argues that the specification, while being enabling for a method of determining whether a mammalian subject is suffering from or at risk for developing pancreatic cancer which method comprises testing a pancreatic biopsy or pancreatic cell culture or pancreatic juice sample but does not reasonably provide enablement for testing any and all biological sample obtainable from a human subject." (Office Action, p.3) Applicants respectfully traverse the rejection.

While in no way acquiescing to any validity of the Examiner's rejection, and solely in the interest of expediting prosecution and allowance of the claims, Applicants

have amended the claims. The present claims recite that the sample is a pancreatic cell culture, a pancreatic tissue biopsy or a pancreatic juice sample.

Accordingly, Applicants respectfully request that the rejection be withdrawn.

35 USC 112, Second Paragraph

Claims 1 – 2, 4, 8 – 11, 13 – 14 and 17 and 24 have been rejected under 35 USC 112, second paragraph as being allegedly indefinite. (Office Action, p.5). Applicants respectfully traverse the rejection.

The Examiner argues that "claims 1 and 24 are indefinite as regards the scope of the claimed invention. Claims 1 and 24 recite the phrase 'a variant thereof', then recites that the 'methylated SPARC nucleic acid molecule comprise at least about 90% sequence identity to the nucleic acid sequence set forth in SEQ ID NO:1.'" (Office Action, p.5). The Examiner questions if "the limitation relate(s) to both SPARC nucleic acid molecule and variants thereof or to only the SPARC nucleic acid molecule…(and) it is unclear the to the Examiner what is intended by the phrase at least about 90% identity or at least about 95% identity." (Office Action, p.5). The Examiner also indicates that "it is unclear to the Examiner what is intended by the phrase 'at least about five fold'….and 'at least about ten fold.'" (Office Action, p.5).

While in no way acquiescing to any validity of the Examiner's rejection, and solely in the interest of expediting prosecution and allowance of the claims, Applicants have amended the claims.

The present claims recite a method for diagnosing pancreatic cancer, comprising the detection of a methylated SPARC nucleic acid molecule in a sample from a subject, wherein the methylated SPARC nucleic acid molecule has at least 90% sequence identity to the nucleic acid set forth in SEQ ID NO: 1 (Figure 6), and wherein the sample is a pancreatic cell culture, a pancreatic tissue biopsy or a pancreatic juice sample. (Claim 1). The claims recite a method for diagnosing pancreatic cancer, comprising the detection of a methylated SPARC nucleic acid molecule in a sample from a subject, wherein the nucleic acid molecule is expressed at least 5 fold lower in a patient with pancreatic cancer as compared to expression in a normal individual, and wherein the

methylated SPARC nucleic acid molecule has at least 90% sequence identity to the nucleic acid set forth in SEQ ID NO: 1 (Figure 6), and wherein the sample is a pancreatic cell culture, a pancreatic tissue biopsy or pancreatic juice sample. (Claim 24).

Accordingly, the claims clearly point out and claim the subject matter which Applicant regards as the invention.

Applicants respectfully request that the rejection be withdrawn.

35 USC 102(b)

Claims 1, 4, 8, 13 – 14, 17 and 24 have been rejected under 35 USC 102(b) as being anticipated by Schutte (Cancer Research 57: 3126 – 3130(1997)). Applicants respectfully traverse the rejection.

The present claims have been set forth above.

The Examiner argues that "Schutte et al. teach a method of diagnosing pancreatic cancer which comprises detecting the methylation of CpG residues in the promoter region of the p16 gene (i.e. a variant of the SPARC gene)." (Office Action, p.6). The Examiner argues that "Schutte et al. teach a method of diagnosing pancreatic cancer which comprises detecting the methylation of CpG residues in the promoter region of the p16 gene (i.e. a **variant** of the SPARC gene)." (Office Action, p.7; emphasis added).

To anticipate a claim, each and every element of the claim must be found in a single reference. This is discussed in the Manual of Patent Examining Procedure § 2131:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the . . . claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226,

> 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an ipsissimis verbis test, i.e., identity of terminology is not required. In re Bond, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

The Schutte reference does not teach or suggest all the limitations of the instant claims. As pointed out by the Examiner, the Schutte reference teaches detecting the methylation of CpG residues in the promoter region of a variant of the SPARC gene. The Schutte reference examines expression of p16 in pancreatic carcinoma cell lines, and examines transcriptional silencing of the p16 gene in association with methylation. Nowhere does the Schutte reference teach or suggest detection of a methylated SPARC nucleic acid molecule that has at least 90% sequence identity to the nucleic acid set forth in SEQ ID NO: 1.

Based on the foregoing, Applicants submit that the claims are not anticipated by the Schutte reference.

Applicants respectfully request withdrawal of the rejection and allowance of the claims.

Claims 1 – 2, 4, 8 – 9, 13 – 14, 17 and 24 have been rejected under 35 USC 102(b) as being anticipated by Goggins et al. [US2007/0015156] or Goggins et al. [US 2003/0190616]. Applicants respectfully traverse the rejection.

The present claims have been set forth above.

The Examiner argues that "Goggins teaches a method of diagnosing pancreatic cancer which comprises detecting the methylation status of CpG residues in the promoter region of selected genes…any of which could be a variant of the SPARC gene." (Office Action, p.8).

To anticipate a claim, each and every element of the claim must be found in a single reference (MPEP § 2131).

The Goggins reference does not teach or suggest all the limitations of the instant claims. In particular, the Goggins reference does not teach or suggest a method for diagnosing pancreatic cancer, comprising the detection of a methylated SPARC nucleic acid molecule in a sample from a subject, wherein the methylated SPARC nucleic acid molecule has at least 90% sequence identity to the nucleic acid set forth in SEQ ID NO: 1, as claimed.

The Goggins reference (US2007/0015156) is directed to methods for detecting pancreatic carcinoma in a subject comprising: a) contacting a nucleic acid-containing specimen from the subject with an agent that provides a determination of the methylation state of at least one gene or associated regulatory region of the gene; and b) identifying aberrant methylation of regions of the gene or regulatory region. The Goggins reference teaches that the genes are selected from CDH3, reprimo, CLDN5, DR3, FOXE1, LDOC1, LHX1, NEFH, NPIX2, PIG11, SARP2, ST14, SMARCA1, TJP2, UCHL1, WNT7A, or a combination thereof. Nowhere does the Goggins reference teach or suggest detection of a methylated SPARC nucleic acid molecule that has at least 90% sequence identity to the nucleic acid set forth in SEQ ID NO: 1.

Based on the foregoing, Applicants submit that the claims are not anticipated by the Schutte reference.

Applicants respectfully request withdrawal of the rejection and allowance of the claims.

35 USC 103(a)

Claims 2 and 9 – 11 have been rejected under 35 USC 103(a) as being unpatentable over Schutte (as above) as applied to claim 1, and further in view of Shuber (US 2003/0087258). (Office Action, p.10). Applicants respectfully traverse the rejection.

The present claims have been set forth above. Claim 2 depends from claim 1, and recites that the presence of a methylated SPARC nucleic acid molecule is compared to a sample from a subject without cancer.

The Examiner argues that "Schutte et al.… teach a method for diagnosing pancreatic cancer comprising all of the limitations of claim 2 except these authors do not teach comparing the methylation pattern obtained from a subject…to sample from a subject without cancer." (Office Action, p.10 – 11). The Examiner argues that "Schutte et al. teach analyzing the methylation pattern of the p16 promoter region of HeLa cells but fail to teach analyzing sample(s) from a subject without cancer. However Shuber teach a method of diagnosing CRC by investigating the methylation status of certain genes wherein the methylation status of said genes in cancer biopsy sample is compared to the methylation status of said genes in individuals without cancer." (Office Action, p.11).

For the reasons discussed above, the Schutte reference does not teach or suggest the present invention as claimed. Nowhere does the Schutte reference teach or suggest detection of a methylated SPARC nucleic acid molecule that has at least 90% sequence identity to the nucleic acid set forth in SEQ ID NO: 1. The Shuber reference does not make up for the flaws of the Schutte reference. The Shuber reference teaches amplification-based methods for detecting hypermethylated nucleic acid in heterogeneous biological samples. According to preferred embodiments of Shuber, a plurality of target CpG containing regions are tested for the presence of hypermethylation. Preferably, one or more of the following regions are assayed in patient nucleic acid isolated from a heterogeneous biological sample such as stool: HIC1, p14, HLTF, MINT2, and MINT31 regulatory regions.

The Shuber reference does not make up for the flaws pf the Schutte reference. Neither of the references, taken alone or together, teaches or suggests a method for diagnosing pancreatic cancer, comprising the detection of a methylated SPARC nucleic acid molecule in a sample from a subject, wherein the methylated SPARC nucleic acid molecule has at least 90% sequence identity to the nucleic acid set forth in SEQ ID NO: 1, as claimed.

Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

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Respectfully submitted,

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